## REMARKS

Claims 1, 3, 7, 9-16, and 25 are pending in this application. Claims 1, 3, 7, 9-16, and 25 are rejected under 35 U.S.C. § 102(b) for anticipation by, and under 35 U.S.C. § 103(a) for obviousness over, Simkiss et al. (WO 94/02412; hereinafter "Simkiss"). Claims 1, 3, 7, and 9-16 are also rejected for obviousness-type double patenting over claims 13-27 of U.S. Patent No. 6,287,341 (hereinafter "the '341 patent"), claims 1-14 of U.S. Patent No. 6,214,368 (hereinafter "the '368 patent"), claims 1-2 of U.S. Patent No. 6,132,463 (hereinafter "the '463 patent"), claims 1-21 of U.S. Patent No. 6,027,742 (hereinafter "the '742 patent"), and claims 1-9 of U.S. Patent No. 6,331,312 (hereinafter "the '312 patent"). By this reply, Applicants amend claims 1 and 25 and address each of the Examiner's rejections below.

### Support for the Amendment

Support for the amendment to claims 1 and 25 is found in prior claim 5 and the specification on, e.g., page 16, line 23, through page 17, line 28, and on page 19, line 24, through page 20, line 22. No new matter is added by the amendment.

### Rejections under 35 U.S.C. § 102(b)

Claims 1, 3, 7, 9-16, and 25 are rejected under 35 U.S.C. § 102(b) for anticipation by Simkiss. The Examiner states that Simkiss

> discloses an injectable amorphous calcium phosphate that hardens to form bone in vivo...Applicant...argues that the instant claims require *ex vivo* manufacture of a poorly crystalline apatitic calcium phosphate while...[Simkiss] discloses an *in vivo* process. However, the instant claims do not provide such a requirement. Instead the instant claims state that a poorly crystalline apatitic

> calcium phosphate is provided to an implant site. This does not differentiate between *ex vivo* and *in vivo* processes. (Office Action, pp. 3-4.)

Applicants respectfully traverse the present rejection of claims 1, 3, 7, 9-16, and 25 for anticipation by Simkiss. Applicants address the present rejection as it pertains to independent claim 1, and claims dependent therefrom, and independent claim 25.

*Present Claim 1 is Not Anticipated by Simkiss*

The M.P.E.P. § 2131 states "'A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.' *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)."

Simkiss discloses a synthetic bone precursor material composed of an amorphous calcium phosphate (ACP) and a crystallization inhibitor that, following *in vivo* implantation and loss of the crystallization inhibitor from the precursor material due to leaching, slowly transforms into crystalline hydroxyapatite (HA; abstract and, e.g., page 3, lines 2-14). Simkiss states that the "transformation of amorphous material into bone mineral is slow, e.g., taking days, so that it is likely to integrate into normal healing processes" (see page 3, lines 17-20). In contrast, present claim 1, as amended herein, recites providing a poorly crystalline apatitic (PCA) calcium phosphate for implantation that has an injectable or formable consistency for a time greater than about 10 minutes at about 25°C and that hardens within about 10 to 60 minutes at about 37°C. Although Simkiss describes the manufacture of both fast-setting and slow-setting ACP-containing compositions (see page 6, lines 27-32), Simkiss clearly fails to teach or suggest that

these compositions could or should harden in minutes rather than hours or days. Because Simkiss fails to teach or suggest the administration of a PCA calcium phosphate with an injectable or formable consistency that hardens within about 10 to 60 minutes at about 37°C, Simkiss fails to teach or suggest all of the limitations of present claim 1, and claims dependent therefrom.

Furthermore, Simkiss merely discloses the administration of an ACP material, not a PCA calcium phosphate, as is recited in present claim 1, and claims dependent therefrom. Simkiss neither teaches nor suggests 1) the administration of a PCA calcium phosphate material, 2) that the Simkiss ACP material should be transformed to a more crystalline material, such as PCA calcium phosphate or HA, prior to implantation into a subject, or even 3) that transformation of the Simkiss ACP material to a more crystalline material could occur prior to its implantation into a subject due to the presence of the crystallization inhibitor. In fact, the Simkiss ACP material will only harden (in hours or days) to form crystalline HA once the crystallization inhibitor has leached out, which only occurs when the ACP material has been placed in a liquid environment, for example, the bodily fluids of a subject into which the ACP material has been implanted (see page 2, line 28, through page 3, line 14). Therefore, Simkiss fails to teach or suggest providing anything more than an ACP material prior to implantation into a subject. Simkiss instead describes implanting an ACP material that will subsequently convert to a more crystalline HA material, but only after implantation into the subject and diffusion of the crystallization inhibitor present in the ACP material. Simkiss certainly does not teach or suggest providing a PCA calcium phosphate for implantation into a subject, as is recited in present claim 1. For this reason as well, Simkiss fails to teach or suggest all of the elements of present claim 1, and claims

dependent therefrom.

The Examiner argues that the present method of claim 1, and claims dependent therefrom, only requires providing a PCA calcium phosphate to an implant site, and therefore, the present method does not differentiate between providing the PCA calcium phosphate *ex vivo* versus providing a precursor material that subsequently transforms to PCA calcium phosphate *in vivo*. This is incorrect. Present claim 1 clearly recites a two step method, wherein the first step involves providing a PCA calcium phosphate, and the second step involves implanting the PCA calcium phosphate at an implant site. Claim 1 clearly indicates that the PCA calcium phosphate is provided prior to its implantation (i.e., using an *ex vivo* method of preparation), and is not prepared *in vivo* at the implant site by virtue of a chemical reaction that transforms reactants into the PCA calcium phosphate. Simkiss, by contrast, clearly discloses an implanted precursor material (i.e., ACP and a crystallization inhibitor) that only transforms to a crystalline HA *in vivo* following implantation into a subject and exposure of the implanted material to the subject's bodily fluids. Therefore, for all of the above reasons, Simkiss fails to teach or suggest all of the elements of present claim 1, and claims dependent therefrom. Accordingly, Applicants respectfully request that the rejection of claims 1, 3, 7, and 9-16 under 35 U.S.C. § 102(b) for anticipation by Simkiss be withdrawn.

*Present Claim 25 is Not Anticipated by Simkiss*

The Examiner also argues that Simkiss anticipates present claim 25, because Simkiss discloses the use of a synthetic bone precursor material composed of an ACP material and a crystallization inhibitor to assist in the attachment of protheses, in which the precursor material is

provided as a mixture of "fast and slow-setting materials...[that] have not yet set or hardened and this occurs *in vivo*" (Office Action, p. 4).

Applicants have amended claim 25 to recite that the method requires applying a paste comprising an amorphous calcium phosphate and a poorly crystalline apatitic calcium phosphate to a prosthesis that has been introduced to an implant site, in which the paste has a formable or injectable consistency for a time greater than about 10 minutes at about 25°C and hardens within about 10 to 60 minutes at about 37°C. As is discussed above, Simkiss fails to teach or suggest that the fast or slow setting ACP compositions are injectable or formable for greater than about 10 minutes at about 25°C, much less that they harden within about 10 to 60 minutes at about 37°C. Simkiss clearly indicates that the material preferably hardens on the order of days or hours and not minutes. Therefore, Simkiss does not teach or suggest all of the limitations of present claim 25, as amended.

In addition, Simkiss merely describes mixing several amorphous calcium phosphate materials for the purpose of adjusting the rate at which the precursor material hardens *in vivo* (see page 6, lines 12-21). Simkiss fails to teach or suggest the use of a calcium phosphate material other than an amorphous calcium phosphate (e.g., the PCA calcium phosphate recited in present claim 25), or that any of the ACP materials to be used in the Simkiss composition would promote transformation of the Simkiss composition to a crystalline HA material, following implantation into a subject and leaching of the crystallization inhibitor from the Simkiss composition, within about 10 to 60 minutes at 37°C. Therefore, Simkiss fails to teach or suggest the preparation of a paste comprising, in addition to an ACP, a poorly crystalline apatitic calcium phosphate, as is recited in present claim 25. Absent this teaching or suggestion, Simkiss cannot be relied upon as

teaching or suggesting all of the limitations of present claim 25. Therefore, for the reasons provided above, Simkiss fails to teach or suggest all of the elements of claim 25. Accordingly, Applicants respectfully request that the rejection of claim 25 under 35 U.S.C. § 102(b) for anticipation by Simkiss be withdrawn.

Rejections under 35 U.S.C. § 103(a)

Claims 1, 3, 7, 9-16, and 25 are rejected under 35 U.S.C. § 103(a) for obviousness over Simkiss. For the reasons discussed above, Applicants also respectfully traverse this rejection of present claims 1, 3, 7, 9-16, and 25. Applicants again address the rejection as it pertains to independent claim 1, and claims dependent therefrom, and independent claim 25.

*Present Claim 1 is Not Obvious Over Simkiss*

The M.P.E.P. § 2143.03 states:

> To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

As is discussed above, Simkiss fails to teach or suggest a method for treating a bone defect by implanting PCA calcium phosphate having the characteristics recited in present claim 1. Simkiss merely describes implanting a precursor material composed of an ACP and a crystallization inhibitor. Following implantation, the crystallization inhibitor leaches out of the Simkiss precursor material and the remaining ACP slowly transforms into crystallized HA. Simkiss fails to teach or suggest that the ACP material remains injectable or formable for greater than 10 minutes at 25°C, or that it can harden within 10-60 minutes at 37°C. Further, Simkiss

fails to teach or suggest that the ACP material could or should be replaced with a PCA calcium phosphate, that the ACP transformation to crystalline HA should occur prior to implantation, or even that the transformation of the ACP material to a more crystalline HA material could occur prior to its implantation into a subject due to the presence of the crystallization inhibitor, or that it would be preferable for such a transformation to occur prior to implantation of the ACP material into a subject. Absent this disclosure, Simkiss fails to teach or suggest all of the elements of present claim 1, and claims dependent therefrom, and fails to serve as the basis for a rejection of claims 1, 3, 7, and 9-16 under 35 U.S.C. § 103(a) for obviousness. Accordingly, Applicants respectfully request that the rejection of these claims be withdrawn.

*Present Claim 25 is Not Obvious Over Simkiss*

The Examiner also rejects claim 25 for obviousness over Simkiss. As is discussed above, Simkiss fails to teach or suggest a method for embedding a prosthetic device by introducing the prosthetic device at an implant site and applying to the device a paste composed of an amorphous calcium phosphate, a poorly crystalline apatitic calcium phosphate, and a physiologically acceptable fluid, in which the paste remains injectable or formable for greater than 10 minutes at 25°C and hardens at the implant site within 10-60 minutes at 37°C. Simkiss merely describes the use of a composition comprising a mixture of several amorphous calcium phosphate materials and a crystallization inhibitor, not the use of composition comprising an ACP and a PCA calcium phosphate, as is recited in present claim 25. Simkiss also fails to teach or suggest any duration of time, other than hours or days, for hardening of the ACP material following its application to a prosthetic, whereas present claim requires hardening within about 10 to 60 minutes. Because

Simkiss fails to teach or suggest the use of a paste comprising an ACP and a PCA calcium phosphate, or that such a paste has the hardening characteristics of the paste recited in present claim 25, Simkiss fails to teach or suggest all of the limitations of present claim 25. For this reason, Simkiss fails to serve as the basis for a rejection of claim 25 under 35 U.S.C. § 103(a) for obviousness. Accordingly, Applicants respectfully request that this rejection be withdrawn as well.

Obviousness-type Double Patenting Rejection

The Examiner rejects claims 1, 3, 7, and 9-16 for obviousness-type double patenting over claims 13-27 the '341 patent, claims 1-14 of the '368 patent, claims 1-2 of '463 patent, claims 1-21 of the '742 patent, and claims 1-9 of the '312 patent stating:

> Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant methods are either the genus of a claimed species or disclose a claimed composition. Office Action, p. 7.

In the event the pending claims are found to be otherwise allowable, Applicants will consider the appropriateness of filing a terminal disclaimer to overcome this rejection.

## CONCLUSION

In view of the above remarks, Applicants respectfully submit that the claims are in condition for allowance, and such action is respectfully requested.

Enclosed is a petition to extend the period for replying for five months, to and including May 23, 2004, and a check for the fee required under 37 C.F.R. § 1.17(a).

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: May 20, 2004

Paul T. Clark
Reg. No. 30,162

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045